48. Isolated proliferating cells having human nuclear DNA and bovine-derived mitochondria obtained according to the method of Claim 36.

49. Isolated proliferating cells having human nuclear DNA and bovine-derived mitochondria obtained according to the method of Claim 39.

50. Isolated proliferating cells having human nuclear DNA and bovine-derived mitochondria obtained according to the method of Claim 46.

51. A method of producing embryo-derived, proliferating cells having human nuclear DNA and bovine-derived mitochondria, comprising the following steps:

(i) enucleating a bovine oocyte;

(ii) inserting a human epithelial cell or epithelial cell nucleus into the bovine oocyte under conditions suitable for the formation of a nuclear transfer unit;

(iii) activating the resultant nuclear transfer unit;

(iv) culturing the activated nuclear transfer unit to obtain a nuclear transfer unit having at least 16 cells; and

(v) culturing cells comprising the inner portion of the nuclear transfer unit of step (iv) in vitro on a feeder layer of mouse embryonic fibroblasts to obtain cells proliferating as a colony.

52. Isolated proliferating cells having human nuclear DNA and bovine-derived mitochondria obtained according to the method of Claim 51.

REMARKS

This amendment is responsive to the Office Action mailed on August 15, 2002. Claims 1-35 are canceled and new claims 36-52 are submitted. The amendment does not introduce new matter.

Support for the claimed method of producing isolated proliferating cells having human nuclear DNA and bovine-derived mitochondria is found in the specification, for example, on page 9, lines 18-30, and in Example 1. Support for the step of culturing the activated nuclear transfer unit to obtain a multicellular nuclear transfer unit comprising at

least 16 cells as recited in claim 36 is found on page 28, lines 6-14. Support for the claimed method wherein the human cell is selected from the group consisting of epithelial, neural epidermal, keratinocyte, hematopoietic, melanocyte, chondrocyte, B lymphocyte, T lymphocyte, erythrocyte, macrophage, monocyte, mononuclear, fibroblast, cardiac muscle, and non-cardiac muscle cell, as recited in claim 38, is found on page 11, lines 17-27. Support for the claimed method comprising inserting a human cell into the bovine oocyte, and then fusing the human cells and oocyte, e.g., by electrofusion, as recited in claims 41-42, is found, for example, on page 15, lines 8-23. The method wherein the activated nuclear transfer unit is cultured to obtain a nuclear transfer unit comprising about 50 cells, as recited in claim 44, is described on page 19, lines 6-10. Support for culturing the activated nuclear transfer unit on a feeder layer as recited in claim 45 is found in the paragraph bridging pages 18-19.

Regarding rejection of the claims under 35 U.S.C. 101

Claims 18-23 were rejected under 35 USC 101 as reading on a cell that is a human embryo. Claims 18-23 are canceled, and the newly added product claims are limited to proliferating cells having human nuclear DNA and bovine-derived mitochondria that are obtained by a method comprising culturing cells comprising the inner portion of a nuclear transfer unit in vitro to obtain cells proliferating as a colony. The new claims therefore do not encompass a cell that is a human embryo, and withdrawal of the rejection under 35 USC 101 is respectfully requested.

Regarding provisional obviousness-type double-patenting rejection of the claims

Claims of the present application were provisionally rejected for obviousness-type double-patenting over claims of co-pending Application Nos. 09/260,468 and 09/685,061. The Applicants respectfully submit that if at the time that allowance is negotiated, claims in the instant application are found to claim the same invention as claims of the co-pending Applications, Applicants will submit a terminal disclaimer to obviate this rejection. The Applicants' therefore affirm that a terminal disclaimer will be submitted when the claims in the instant application are found to be allowable, but for the outstanding double patenting rejection over claims of co-pending Application Nos. 09/260,468 and 09/685,061. If additional response to the provisional obviousness double patenting rejection is required, it is respectfully requested that the Examiner contact the undersigned so that the issue may be addressed expeditiously.

Regarding rejection of the claims under 35 U.S.C. 112, first paragraph:

The claims were rejected under 35 U.S.C. 112, first paragraph, as being non-enabled by the specification, on the grounds that reprogramming of the donor human nucleus in a non-human oocyte is unpredictable, and the specification does not demonstrate that the product cells have the totipotency or pluripotency of ES cells.

The claims are amended to recite a method for producing embryo-derived, cells having human nuclear DNA and bovine-derived mitochondria that are proliferating as a colony in vitro. The scope of the claims accords with the unexpected discovery, described in Example 1, that such cells can even be produced (see the second paragraph of page 9). The specification teaches that the cells of the present invention are useful for studying cell differentiation and for drug studies (p. 7, lines 20-22). Persons skilled in the art would recognize that the unusual cells produced by the present invention, by virtue of having human nuclear DNA and bovine-derived mitochondria, are useful for studying drugs that target cellular molecules that mediate mitochondria-dependent energy metabolism, and for identifying species-specific aspects of mitochondria-dependent energy metabolism. Persons skilled in the art would also recognize that the cells produced by the present invention are useful for assaying the sensitivity of a human host immune system to transplanted syngenic and allogenic cells containing non-human mitochondria. The extent to which a human transplant recipient will accept or reject transplanted syngenic cells having non-human mitochondria is of great scientific and medical interest (see R.P. Lanza et al., Nature Biotechnology, July 2002, Vol. 20, pp. 689-696). Given the disclosure of a working example of the claimed invention in the application, one skilled in the art would reasonably expect to be able to follow the teachings of the specification and successfully use the claimed method to produce the claimed cells without having to perform undue experimentation. The Applicants therefore respectfully request that the rejection of the claims under 35 U.S.C. 112, first paragraph, for non-enablement be withdrawn.

Regarding rejection of claims under 35 U.S.C. 112, second paragraph:

Claims were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for reciting "embryonic or stem-like cells," "desired," and "DMAP;" which terms are either not used in the present claims, or in the case of DMAP, are defined (as dimethylaminopurine). Accordingly, withdrawal of the rejection for ind finiteness under 35 U.S.C. 112, second paragraph, is respectfully requested.

Regarding rejection of the claims under 35 U.S.C. 102(a), (b) or (e), or 103(a):

The Applicants respectfully submit that none of the cited references describes or suggests practicing the claimed method to make the claimed cells having human nuclear DNA and bovine-derived mitochondria. Moreover, at the time of the invention it was impossible to predict that an NT unit produced by transferring the nucleus of a human cell into a bovine oocyte could be cultured in vitro to produce cells that proliferate in colony fashion. Given the uncertainties of reprogramming, this was an unexpected and non-obvious result. Under U.S. patent law, a suggestion or motivation to combine various teachings of prior art references to obtain the claimed invention, and a reasonable expectation that the combination will operate successfully, must be found in the prior art, not in applicant's disclosure. See M.P.E.P. § 2143, Basic Requirement of a *Prima Facie* Case of Obviousness, citing In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The inventors of the present application are the first to disclose that the claimed method can be used successfully to produce colonies of cells proliferating in vitro that have human nuclear DNA and bovine-derived mitochondria. Given that the claimed invention is neither described nor suggested by the prior art, and that those skilled in the art in view could not have predicted that the claimed invention would operate successfully, the Applicants respectfully request that the rejection of the claims under 35 U.S.C. 102 and 103(a) be withdrawn.

It is believed that the foregoing amendment has fully addressed the points raised in the official action, and that the application is now in condition for allowance. Early notice to this effect is respectfully requested.

Respectfully submitted,
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